

Applicants: Anna Marie Pyle and Eckhard Jankowsky  
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to establish a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim. First, the cited references, when combined, teach or suggest every element of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Applicants maintain that the cited references fail to support a *prima facie* case of obviousness of claims 1-8, in that they fail to create a motive to combine the cited references or a reasonable expectation of success.

The rejected claims provide methods for detecting the release of a single-stranded RNA from an RNA duplex. The instant methods comprise, in relevant part, (a) admixing an RNA helicase with the RNA duplex, wherein the RNA duplex comprises a first RNA having a first label attached thereto and a second RNA, wherein said first label produces a luminescent energy pattern when the first RNA is present in the RNA duplex, which luminescent energy pattern differs from a luminescent energy pattern produced when the first RNA is not present in the RNA duplex; and (b) detecting a change in the luminescent energy pattern produced by the first label so as to thereby detect release of single-stranded RNA from the RNA duplex.

Briefly, Shuman et al., teaches RNA helicase activity from Vaccinia virions by gel electrophoresis. Bjornson et al. teaches a fluorescence-based assay that can be used to monitor helicase-catalyzed unwinding of duplex DNA. Applicants note that nowhere in Bjornson et al. is the word "RNA" even mentioned.

Applicants maintain that the cited references fail to create

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either a motive to combine the cited references or a reasonable expectation of success. In essence, the Examiner concludes that an assay for the study of DNA helicases is predictive of a method for detecting the release of a single stranded RNA from an RNA duplex. In drawing this conclusion, the Examiner takes a quantum and impermissible leap. Simply put, the Examiner maintains that methods involving the detection of unwinding of DNA by DNA helicases would teach or suggest to one skilled in the art methods involving the detection of unwinding of RNA duplexes by RNA helicase. Applicants maintain that this position disregards the well known differences between DNA and RNA. It is undisputed that RNA and DNA are chemically distinct molecules having certain distinct properties.

In support of his argument, the Examiner first cites Shuman et al. which in essence teaches a study of Vaccinia virus RNA helicase. The Examiner concedes that nowhere in Shuman is there even a suggestion of using fluorescent dyes to study RNA helicases or RNA unwinding. Second, the Examiner incorrectly suggests that Bjornson et al. teach that their assay for dsDNA would be "advantageous" in the context of unwinding of RNA duplexes. Applicants note that Bjornson et al. do not mention RNA in its text, and maintains that if the authors had intended to make such a suggestion about RNA unwinding, they could have done so. In essence, Bjornson et al. do not address RNA or RNA unwinding.

The Examiner also rejected claim 6 under 35 U.S.C. §103(a) as allegedly unpatentable over Shuman in view of Bjornson et al. and Vargo et al. (U.S. Patent 6,232,386 B1, issued May 15, 2001).

In response, applicants respectfully traverse the rejection. Applicants' traversal is based, where applicable, on the reasons set forth above and on the following reasons.

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The standard for obviousness is discussed above. Claim 6 provides a method for detecting the release of a single-stranded RNA from an RNA duplex. The instant method comprises, in relevant part, a method wherein the first label is fluorescein isothiocyanate and the second label rhodamine isothiocyanate.

Shuman et al. and Bjornson et al. are discussed above. Briefly, Vargo et al., according to the Examiner, teach the labels fluorescein isothiocyanate and rhodamine isothiocyanate.

Applicants maintain that the cited references fail to create either a motive to combine their respective teachings or a reasonable expectation of success. The Examiner concedes that Shuman et al. in view of Bjornson et al. do not teach the labels fluorescein isothiocyanate and rhodamine isothiocyanate. In addition, applicants note that nowhere do Vargo et al. suggest that the labels fluorescein isothiocyanate and rhodamine isothiocyanate can be used in a method for detecting the release of a single-stranded RNA from an RNA duplex. In support of the rejection, the Examiner suggests that Vargo et al., in column 29, lines 15-33, provide motivation for using the labels fluorescein isothiocyanate and rhodamine isothiocyanate in the claimed method. Applicants maintain that the portion of Vargo et al. relied up on by the Examiner is, at most, a general statement of the usefulness of oxyhalopolymer composites and surface-oxyhalogenated non-halopolymer composites that are refunctionalized with isothiocyanate, and does not suggest any usefulness of these compounds with respect to methods of monitoring nucleic acid release from a duplex. Applicants point out that the specific text in Vargo et al. quoted by the Examiner merely suggests usefulness for "... probes and sensors, such as for nucleic acids". It does not suggest the use of oxyhalopolymer composites and surface-oxyhalogenated non-halopolymer composites that are refunctionalized with isothiocyanate to label nucleic acids.

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Finally, applicants maintain that the Examiner has mischaracterized their argument with regards to the Vargo reference. The Examiner argues that applicants maintain that Vargo has a different motivation than that of applicants. Applicants maintain, for the reasons set forth above, that Vargo provides no motivation to combine the teachings of Shuman and Bjornson.

In view of the above remarks, applicants maintain that the Examiner has failed to set forth a *prima facie* case of obviousness, and that accordingly, claims 1-8 satisfy the requirements of 35 U.S.C. §103(a).

Conclusion

Applicants maintain that pending claims 1-8 are in condition for allowance, and respectfully request allowance of these claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

*2/21/03*  
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